

**WHAT IS CLAIMED IS:**

1. A rodent neutralizing monoclonal antibody specific for human interleukin-18 and having a binding affinity characterized by a dissociation constant equal to or less than about  $3.9 \times 10^{-11}$  M.
2. The monoclonal antibody according to claim 1 which is a rat monoclonal antibody.
3. The monoclonal antibody according to claim 1 which is a murine monoclonal antibody.
4. The monoclonal antibody according to claim 2 which comprises the light chain amino acid sequence of SEQ ID NO: 1, and the heavy chain amino acid sequence of SEQ ID NO: 9.
5. The monoclonal antibody according to claim 3 which comprises the light chain amino acid sequence of SEQ ID NO: 17 and the heavy chain amino acid sequence of SEQ ID NO: 25.
6. The monoclonal antibody according to claim 2 which comprises the light chain amino acid sequence of SEQ ID NO: 33 and the heavy chain amino acid sequence of SEQ ID NO: 41.
7. The monoclonal antibody according to claim 1 having the identifying characteristics of 2C10, 14B7 or 13G9.
8. A hybridoma which produces the monoclonal antibody of claim 4.
9. A hybridoma which produces the monoclonal antibody of claim 5.
10. A hybridoma which produces the monoclonal antibody of claim 6.
11. A hybridoma having the identifying characteristics of cell line 19522C10(2)F2(1)A1, 195214B7(1)H10 and 187413G9(3)F12

12. A neutralizing Fab fragment or F(ab')<sub>2</sub> fragment thereof, produced by deleting the Fc region of the monoclonal antibody of claim 1.

5 13. An altered antibody comprising a heavy chain and a light chain, wherein the framework regions of said heavy and light chains are derived from at least one selected antibody and the amino acid sequences of the complementarity determining regions of each said chain are derived from the monoclonal antibody of claim 1.

10 14. An immunoglobulin light chain complementarity determining region (CDR), the amino acid sequence of which is selected from the group consisting of:

- (a) SEQ ID NO: 3
- (b) SEQ ID NO: 5
- 15 (c) SEQ ID NO: 7
- (d) SEQ ID NO: 19
- (e) SEQ ID NO: 21
- (f) SEQ ID NO: 23
- (g) SEQ ID NO: 35
- 20 (h) SEQ ID NO: 37
- (i) SEQ ID NO: 39

25 15. An immunoglobulin heavy chain complementarity determining region (CDR), the amino acid sequence of which is selected from the group consisting of:

- (a) SEQ ID NO: 11
- (b) SEQ ID NO: 13
- (c) SEQ ID NO: 15
- (d) SEQ ID NO: 27
- 30 (e) SEQ ID NO: 29
- (f) SEQ ID NO: 31
- (g) SEQ ID NO: 43
- (h) SEQ ID NO: 45
- (i) SEQ ID NO: 47

35 16. A nucleic acid molecule encoding the immunoglobulin complementarity determining region (CDR) of claim 14.

17. A nucleic acid molecule encoding the immunoglobulin complementarity determining region (CDR) of claim 15.

5 18. A pharmaceutical composition comprising the altered antibody of claim 13 and a pharmaceutically acceptable carrier.

10 19. A method of treating conditions associated with autoimmune disease comprising the step of administering to said human in need thereof an effective amount of the altered antibody of claim 13.

20. The method of claim 19 where said disease is multiple sclerosis.

15 21. The method of claim 19 where said disease is rheumatoid arthritis type I or insulin dependent diabetes.

22. The method of claim 19 where said disease is inflammatory bowel disease.

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23. The method of claim 19 where said disease is psoriasis.

24. An isolated nucleic acid sequence which is selected from the group consisting of:

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- (a) a nucleic acid sequence encoding the altered antibody of claim 13
- (b) a nucleic acid sequence complementary to (a); and
- (c) a fragment or analog of (a) or (b), which encodes a protein, characterized by having a specificity for human interleukin-18; wherein said sequence optionally contains a restriction site.

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25. A method to assess the presence or absence of human IL-18 in a human which comprises obtaining a sample of biological fluid from a patient and allowing the monoclonal antibody of claim 1 to come in contact with such sample under conditions such that an IL-18/monoclonal antibody complex can form and detecting the presence or absence of said IL-18/monoclonal antibody complex.

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26. A method for aiding in the diagnosis of autoimmune disease associated with comprising the steps of determining the amount of human IL-18 in a sample of a patient according to the method of claim 25 and comparing that to the mean amount of human IL-18 in the normal population, whereby the presence of
- 5 significantly elevated amount of human IL-18 in the patient is an indication of autoimmune disease.